

**POLYPOUS RHINOSINUSITIS: ALTERATIONS  
OF LOCAL ADAPTIVE IMMUNITY**

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**Abstract.** The etiology and pathogenesis of PRS remain unclear. Many works in this direction did not change the situation. However, ideas about the pathogenesis of PRS have recently undergone significant changes, primarily due to advances in the field of clinical immunology of ENT diseases. In all theoretical views on the genesis of nasal polyps, the involvement of the immune system, especially the immune status of the nasal mucosa, plays a leading role.

**Key words.** Chronic polyposis rhinosinusitis, sinus surgery, endoscopy, FESS operations.

**Enter**

Therefore, in accordance with the decisions of international consensus conferences, PRS is figuratively defined as "nasal asthma" using all the terms of modern immunology related to the immunopathogenesis of this process. Analysis of special literature and dissertation studies on the structure of the paranasal sinuses, especially the ethmoid labyrinth, the role of genetic factors and bacterial biofilms in the development of chronic rhinosinusitis, the characteristics of the pathophysiological processes occurring in the cells of the ethmoid labyrinth. during ethmoiditis and in the body as a whole led to turning to various scientific sources at the intersection of different disciplines: rhinology, radiology, microbiology, allergology, genetics, cytology.

**The purpose of the study**

Thus, it is clear from the presented modern literature that changes in local immunity in PRS are multifaceted. The complexity and interdependence of immunopathogenetic mechanisms determines the insufficient clinical effectiveness of immunotropic therapy. However, these changes are the target of current drug treatments. At the same time, these "points of action" are the subject of the development of new drugs with anti-inflammatory and immunomodulatory effects.

**Changes in local adaptive immunity**

In the current literature, much attention is paid to the local immune status in PRS. The results of these studies can be divided into two blocks - data block on adaptive local immunity and data block on innate local immunity. In the first case, we talk about the CD phenotype of the cells in the inflammatory infiltrate, the expression

of inflammatory genes, cytokines, chemokines, growth factors, adhesion factors and angiogenesis by activated cells. In the second case, the expression of innate immune receptors in the same cells is studied, first of all, it is the above-mentioned Toll -, Rig -, Nod - and other receptors [3,9]. The close functional relationships between these two compartments of the immune system are well known [12]. However, given the subject of this work, it is necessary to present the most recent, most interesting scientific data on changes in local adaptive immunity in PRS. The importance of these data is that the correction of immunopathological processes occurring in the area of nasal polyps consists in the creation of local anti-inflammatory and/or immunotropic therapy schemes. The interpretation of available data on this issue is as uncertain as the interpretation of changes in systemic adaptive immunity in PMS. However, the relationship between systemic and local adaptive immune indicators allows interpretation of changes in the immune status in terms of typical changes in the cells of the peripheral blood immune system in situ.

But first, it must be said that the migration of cells from peripheral blood to inflammatory tissues is governed by a precise sequence of events. These events are mediated by two types of signals: diffusible chemotactic factors and cell surface adhesion factors. Under the influence of sensitizing inflammatory signals, leukocytes turn in the endothelium due to the expression of selectins and the corresponding ligands in leukocytes, then these cells migrate to the tissues of nasal polyps and take an active part in the pathological process. process [12].

It leads to hyperproduction of ESP, MBP, eotaxins 1, 2, 3, growth factors (TGF- $\beta$ ), angio- and neoangiogenesis factors (VEGFs, VEGF-A, VEGF-B), chemokines (RANTES, Eotaxin), adhesion molecules (ICAM-1, VCAM-1, E-selectin, P-selectin) and secondly, to activate cells, primarily the immune system. situ and the active participation of these cells in the formation of inflammation in the nasal mucosa [9,12,15]. According to modern concepts, eosinophils, which produce anti-inflammatory factors, in turn activate fibroblasts and platelets, in which the synthesis of growth factors is uncontrolled in conditions of chronic inflammation. We are talking about transforming growth factor- $\beta$  (TGF- $\beta$ ), platelet (PDGF) and epithelial (EGF) growth factors that disrupt the integrity of the collagen structure of the nasal mucosa and lead to its reconstruction [9,16,16]. The participation of activated T-lymphocytes (CD 3+ CD 45 RO +), B lymphocytes (CD 20+ cells), plasma cells, IgE receptor-carrying mast cells and others has been shown in these processes [9,13]. Concentrations of IL-5 and IL-5 receptor, the main cytokine responsible for the activation and accumulation of eosinophils at the site of inflammation, were 1200-fold higher in patients with PRS compared to controls [10].

From the point of view of the pathogenesis of PRS, very important information is provided by the phenotype of inflammatory infiltrate cells. IGX methods showed that the level of B cells (CD 19+ and CD 20+) and plasma cells (

CD 138+ ) in the tissues of nasal polyps was significantly higher than similar values in the group of patients with chronic rhinosinusitis. was high and these. facts related to production intensity in situ Enterotoxin-specific IgE, IgG 4 and IgA St. aureus [16]. These results are consistent with the results of a study conducted by Japanese authors. According to these data, a significant increase of PRS-activated CD 20+ cells (B-lymphocytes) is detected in the area of nasal polyps, which is the result of protein synthetic activity, as well as an increase in their concentration. Production of Ig in situ of all classes, tumor necrosis factor (TNF) family, and B-cell activating factor (BAFF) with anti-inflammatory properties [11]. In nasal polyps, the number of cells with surface markers of T-lymphocytes predominated over B-lymphocytes. A characteristic feature of the topography of the latter is that they showed a clear tendency to perivascular localization [13]. Among the subpopulations of T helper cells (CD 4+), that is, Th -1 and Th -2 types in PRS, the percentage of Th -2 CD 4+ cells was statistically significantly increased in the group of PRS patients with clinical signs of atopy. The distribution of this subpopulation of CD 4+ cells in nasal polyp tissue has also been shown in other studies by leading researchers on the PRS problem [14]. Pro-inflammatory cytokines such as IL-6 and its receptors produced by nasal epithelial cells have been shown to be actively involved in the pathogenesis of PRS. We talk about the fact that the synthesis of these inflammatory factors is triggered by infectious "triggers" PRS - Staphylococci. aureus and Pseudomonas aeruginosa [11]. At the same time, the study of a wide range of CD phenotype of inflammatory infiltrate cells in the nasal mucosa and nasal polyps ( CD 1+, CD 2+, CD 3+, CD 5+, CD 7+, CD 4+, CD 8+ ). , CD 10+, CD 20+, CD 19+ and HLA - DR +) did not show significant differences [14].

A review [10] analyzed the results of studies of inflammatory genes in PRS, which showed that gene expression of the above cytokines, chemokines, and growth factors plays an important role in the persistence of inflammation in the nasal cavity. Mucous membrane in PRS.

In PRS, the functional state of a group of zinc-containing enzymes - endopeptidases with proteolytic activity against some components of the extracellular matrix of connective tissue - is important in the process of nasal mucosa reconstruction. These enzymes are called matrix metalloproteinases (MMPs), which generally play an important role in remodeling the body's connective tissue [11,12,13]. In PRS, the ratio of MMPs and tissue inhibitors of their activity (TIMPs) was significantly changed compared to the control group [11]. In nasal polyp tissue, the expression of MMPs such as MMP-2 and MMP-9 in endothelial cells and epithelial cells was increased. The activity of this type of MMPs (in the sense of proteolysis) is focused on type 4 collagen, which forms the framework of connective tissue. Similar results were obtained by other authors regarding MMP-2, MMP-7, MMP-9 and TIMP-1 in PRS and chronic rhinosinusitis [114,119,120]. The data

presented are interesting in that they show some pathogenetic similarity between systemic connective tissue diseases and PRS. It is known that the pathogenesis of systemic connective tissue diseases is largely related to the activity of MMPs, and the process of connective tissue remodeling in these diseases and the tissue of nasal polyps in PRS have certain similarities.

In the context of the interaction of cells in the inflammatory infiltrate in PRS and based on their own data, Japanese authors hypothesized that mast cells of the nasal mucosa and activated eosinophils (CD 34+) in the inflammatory infiltrate in the nasal cavity . polyps cooperate to cause subsequent migration of eosinophils from blood vessels to tissues, and this process is simultaneously regulated by the functional activity of fibroblasts. The latter, among others, produces transforming growth factor (TGF- $\beta$ ), which, in turn, stimulates the expression of vascular endothelial growth factor (VEGF), which is the main factor in angiogenesis and tumor development in nasal polyps. strengthens In addition, according to the authors, eosinophil basic protein ( MBP ) and eosinophil cationic protein ( ECP ) released from in situ activated eosinophils are actively involved in effective inflammation [1]. Recurrence of nasal polyps after nasal polypotomy is undoubtedly one of the most important aspects of the PRS problem. To date, the scientific basis of the recurrence of nasal polyps has not been developed and is not understood. Based on these rules, we analyzed our data on the state of adaptive immunity of patients with PRS according to relapses. The results of the analysis are presented in this part of the work.

As mentioned above, we examined 38 patients with PRS. 20 of them had recurrent polyposis, which is 52% of the total group. According to the history of the disease, the frequency of relapses varies from 1-2 to 6-7. Relapses occurred in 100% of patients with a disease duration of more than 5 years, 57% of cases from 1 to 5 years, and no relapses occurred in patients with a disease duration of up to 1 year. all. Interestingly, in the group of patients with eosinophilia more than 150 cells /  $\mu$ L, the relapse rate was three times higher than in patients with eosinophilia up to 150 cells /  $\mu$ L (81.6% vs. 30%). Regarding the pathomorphology of nasal polyps, differences were insignificant in patients with fibro-edematous type, there was a tendency to increase the frequency of relapses; It should also be noted that BA occurred only in patients with the recurrent type of PRS, that is, in 27.2% of cases.

In accordance with the material presentation plan adopted in this work, we first present ICH data on the composition of the inflammatory infiltrate. The density of CD-positive cells in the tissues of nasal polyps is shown depending on PRS relapses. It can be seen that there were no statistically significant differences between the groups of patients with or without relapses of nasal polyps in any parameter. In control preparations of intact mucosa, CD -positive cells ranged from isolated cases to their complete absence. It can be seen that the inflammatory process in PRS is accompanied

by intensive infiltration of nasal polyp tissue with CD-positive cells, regardless of the recurrence of nasal polyps.

In the group of patients without recurrent nasal polyps, only the percentage of IgA-positive cells increased significantly, but compared to the group of patients with recurrent nasal polyps ( $p < 0.05$ ), i.e. the fact of the recurrence of the disease is directly related to the reliable and significant inhibition of IgA-positive cells. At the same time, these data show the prospects of targeted stimulation of the functional activity of IgA-positive cells to correct changes in the adaptive immune status of patients with PRS. In general, the increase in fluorescence and the number of IgA-positive cells in the peripheral blood of patients with PRS indicate the unconditional activation of this type of cells responsible for the formation of systemic and, in particular, local humoral immunity (sIgA)-positive cells). Regarding IgG- and IgM-positive cells, the changes in the studied properties of these cells were unreliable in both groups.

The relationship between the studied indicators is shown in the table. As can be seen from the table, in the group of patients with recurrent polyps, a significant negative strong correlation was found only with respect to CD 68+ cells. In the group of patients without recurrence of nasal polyps, a significant positive average correlation was found with respect to CD 8+ and CD 68+ cells, and in the latter case this relationship was accompanied by a significant increase in the level of these cells in the blood compared to the control group (Table 15). In other words, in the group of patients with non-relapsing PRS, there is a simultaneous increase in the level and functional activity of CD 68+ cells both in the peripheral circulation and in the inflammatory infiltrate in nasal polyps.

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